REMARKS

Claims 1-66 are pending in this application. Claims 12-55 are withdrawn from further consideration as being drawn to a nonelected subject matter. Claims 1-10 and 56-66 were rejected under 35 U.S.C. § 112, first paragraph. Claims 1-11 and 56-66 were variously rejected under 35 U.S.C. § 112, second paragraph. Claims 1-7 and 9-11 were variously rejected under 35 U.S.C. § 102(b).

By this amendment, claims 1 and 56 have been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification, for example, at page 37, lines 9-10.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1-11 and 56-66 were rejected under 35 U.S.C. §112, first paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

The Examiner states that "the metes and bounds of the term "linked to" cannot be determined (is this covalent?)." Office Action, page 3.

Applicants respectfully submit that the specification provides a clear measure of what Applicants regard by the term "linked to." For example, the specification states that the "IMP may be covalently or non-covalently linked to the microcarrier in the complex" and that "IMP/MC complexes may be covalent complexes, in which the IMP portion of the complex is covalently bonded to the MC, either directly or via a linker (*i.e.*, indirectly), or they may be non-covalent complexes." Specification, page 6, lined 15-16, and page 19, line 28, to page 20, line 3. Also, at page 37, lines 13-14, the specification states that the "bond between the IMP and MC may be covalent or non-covalent." In addition, Applicants respectfully point out that pages 37-41 provide methods and means by which the IMP and MC of the claimed invention can be covalently or non-covalently linked.

Accordingly, Applicants respectfully submit that the term "linked to" does not render the claimed invention indefinite and that the claims are sufficiently definite when considered in view of the specification and the understanding of those of skill in the art.

With regard to claims 1 and 56, the Examiner states that "the term "sequence 5'-C,G-3'" is unclear (e.g. does this refer to contiguous sequences with a 5' to 3' orientation, or to non-contiguous sequences?)." Office Action, page 4.

Applicants respectfully point out that, as commonly known in the art, the conventional way to indicate the particular arrangement of contiguous nucleotides in a nucleic acid molecule is to bracket the specific nucleotide sequence with a " 5' " and a " 3'." The 5' is used to indicate the free 5' hydroxyl or phosphate at one end of the nucleic acid molecule and the 3' is used to indicate the free 3' hydroxyl group at another end of the nucleic acid molecule. Thus, the phrase "the ISS comprises the sequence 5'-C,G-3" of claims 1 and 56 indicates that the claimed polynucleotide contains a sequence with a contiguous cytosine, guanosine in a 5' to 3' orientation relative to each other.

Accordingly, Applicants respectfully submit that the term "sequence 5'-C,G-3'" does not render the claimed invention indefinite and that the claims are sufficiently definite when considered in view of the specification and the understanding of those of skill in the art.

Applicants also submit that the same explanation holds for the term "5'-T, C, G-3" in claims 9 and 64 and for the term "5'-purine, purine, C, G, pyrimidine, pyrimidine-3'" in claims 10 and 65. For example, at page 21, lines 3-4, the specification states that in some embodiments, "an ISS comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine-3' (such as 5'-AACGTT-3')." The 5'-AACGTT-3' clearly provides an example of a nucleic acid sequence with particular nucleotides in a specific order and orientation relative to each other.

Thus, Applicants respectfully submit that the terms "5'-T, C, G-3" and "5'-purine, purine, C, G, pyrimidine, pyrimidine-3'" do not render the claimed invention indefinite and that the claims are sufficiently definite when considered in view of the specification and the understanding of those of skill in the art.

With regard to the term "liquid phase carrier" of claim 4, Applicants respectfully point out that water-insoluble, liquid phase particles are well known in the art and are described in the specification. The specification provides the requested explanation for how a "particulate composition which is insoluble in water" can be a liquid phase carrier. For example, at page 12, lines 11-18, the specification describes that such microcarriers may be oil or lipid based and may be droplets or micelles found in oil in water or oil in water in oil emulsions. Thus, particles insoluble in water and aqueous solutions but yet liquid in nature are well known.

With regard to the rejection of claim 7 as allegedly not further limiting than claim 6, Applicants respectfully traverse this rejection. The size of the microcarrier in claim 6 is in a range from 10 nm to 10 μm. The size range of the microcarrier in claim 7 is narrower than that in claim 6, *i.e.*, from 25 nm to 5 μm. Since the extent of microcarrier size of claim 7 falls within and is less than the microcarrier size range of claim 6, claim 7 is narrower in scope than claim 6.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-10 and 56-66 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The claimed invention is directed to complexes which comprise an immunomodulatory polynucleotide (IMP) linked to a nonbiodegradable microcarrier. The IMP comprises an immunostimulatory sequence (ISS) and the ISS comprises the sequence 5'-CG-3'. The claimed invention is also directed to kits comprising such complexes.

The Examiner asserts that the specification and claims "do not indicate what distinguishing attributes are concisely shared by the members of the genus comprising immunomodulatory polynucleotide components comprising an immunostimulatory sequence comprising 5'-C, G-3', or 5'-purine-purine-C, G-pyrimidine-pyrimidine-3', or 5'-T, C, G-3' " and that concise structural features that could distinguish compounds within this genus "are missing from the disclosure." The Examiner also asserts that "the disclosure fails to provide a representative number of species to describe the broad genus claimed." Office Action, pages 5-6. Applicants respectfully disagree with these assertions.

The common attribute or characteristic concisely identifying members of the genus of ISS of the claimed invention is that all the ISS include the sequence 5'-C-G-3'. The specification states that the ISS of the invention "can be any length greater than 6 bases or base pairs and generally comprises the sequence 5'-cytosine, guanine-3'." That this is the common attribute of the genus is reflected not only in this statement but also in the structure of the claims. In the independent and broadest claims (claims 1 and 56), the ISS comprises the sequence 5'-C-G-3'.

Depending from these claims are claims in which the ISS comprises 5'-T-C-G-3' or 5'-purine-purine-C, G-pyrimidine-pyrimidine-3'. As can be seen, the sequence 5'-C-G-3' is an essential feature of any ISS of the claimed invention.

Although this genus may include a broad array of ISS, this does not indicate that Applicants were not in possession of the claimed invention or that the specification fails to disclose a representative number of species. The specification, for example at pages 20 to 23, provides many examples of ISS sequences within the claimed genus for use in the present invention. In addition, immunostimulatory polynucleotides comprising the sequence 5'-C-G-3' were well known in the art at the time of filing, as indicated by the many references cited, for example, on pages 4 and 5 of the specification.

In U.S. Pat. No. 6,498,148 (filed January 21, 1999; "the '148 patent"), for example, the invention is directed to a method of treating asthma in which an immunostimulatory polynucleotide is administered to an individual where the immunostimulatory polynucleotide comprises an ISS and the ISS comprises the sequence 5'-cytosine-guanine-3'. In dependent claims of the '148 patent, the ISS comprises additional sequences, for example, 5'-AACGTT-3' and 5'-purine-purine-C, G-pyrimidine-pyrimidine-3'. In the '148 patent, the structure of the ISS is an oligonucleotide 6 bases or greater in length containing a 5'-C-G-3' sequence. Additional examples of ISS sequences useful for the claimed invention are also provided. Thus, the genus of immunostimulatory sequences comprising a 5'-C-G-3' sequence was known in the art when the instant application was filed.

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, e.g., *In re Marzocchi* 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971); MPEP §2163.04. Applicants respectfully submit that the Examiner has not met the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in the instant disclosure a description of the invention defined in the claims.

Thus, Applicants respectfully submit that a *prima facie* case for lack of written description has not been established. Applicants respectfully submit that the written description requirement has been met.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. §102(b)

Claims 1, 3, and 6-9 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sonehara *et al.* (1996, *J. Interferon and Cytokine Res.* 16:799-803; "Sonehara"). Claim 1-7, and 9-11 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Schwartz *et al.* (WO 98/55495; "Schwartz"). Applicants respectfully traverse these rejections.

The claimed invention is directed to a complexes comprising an ISS-containing immunomodulatory polynucleotide (IMP) linked to a non-biodegradable microcarrier (MC). As described on page 37, lines 9-11, of the specification, "IMP/MC complexes comprise an IMP bound to the surface of a microcarrier (i.e., the IMP is not encapsulated in the MC)." Accordingly, the claims have herein been amended to more clearly indicate that the IMP is linked to the surface of the microcarrier.

For a claim to be anticipated by a reference, the reference much teach each and every element of the claim. As discussed below, neither of the cited references teach ISS-containing polynucleotides linked to the surface of a nonbiodegradable microcarrier, *i.e.*, not encapsulated in the microcarrier. Accordingly, Applicants respectfully submit that the references do not anticipate the claimed invention.

Sonehara

Sonehara describes hexamer palindromic oligonucleotides encapsulated in cationic liposomes made with Lipofectin® reagent (page 799, right column, and page 800, left column). Sonehara does not describe a complex in which an immunomodulatory polynucleotide (IMP) is

linked to a microcarrier, much less a complex in which an IMP is linked to the surface of a non-biodegradable microcarrier.

Since Sonehara does not teach each and every element of the claimed invention, Sonehara does not anticipate the claimed invention.

Schwartz

Schwartz describes co-administration of an ISS, antigen and adjuvant, where the adjuvant includes emulsions, alum, liposomes and microparticles. Schwartz, for example, page 15, lines 10-18. Schwartz also describes compositions comprising an ISS, an immunomodulatory molecule and an encapsulating agent in the form of emulsions, microparticles and/or liposomes and "adjuvant oil-in-water emulsions, microparticles and/or liposomes encapsulating an ISS-immunomodulatory molecule in the form of particles." Schwartz, page 15, line 38, to page 16, line 2.

Although Schwartz describes mixtures of ISS with antigen and adjuvant, including microcarriers, Schwartz does not describe a complex in which an IMP is linked to a microcarrier, much less a complex in which an IMP is linked to the surface of a non-biodegradable microcarrier.

Since Schwartz does not teach each and every element of the claimed invention, Schwartz does not anticipate the claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b).

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CONCLUSION

Applicants have, by way of the amendments and remarks presented herein, addressed all issues that were raised in the outstanding Office Action. Applicants respectfully contend that this Amendment and Response has overcome the rejections and that the pending claims are in condition for allowance. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant(s) petition(s) for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882001700.

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Respectfully submitted,

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